Search Results -

Term	Documents
(8 SAME 2).USPT,PGPB,JPAB,EPAB,DWPI.	99

Database: US Patents Full-Text Database
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JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Refine Search: L2 SAME L8 Clear

Search History

Today's Date: 7/14/2001

DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI	L2 SAME L8	99	L9
USPT,PGPB,JPAB,EPAB,DWPI	L7 WITH L1	286	L8
USPT,PGPB,JPAB,EPAB,DWPI	RECEPTOR$	99201	L7
USPT,PGPB,JPAB,EPAB,DWPI	RRECEPTOR$	2	L6
USPT,PGPB,JPAB,EPAB,DWPI	L3 SAME L4	11	L5
USPT,PGPB,JPAB,EPAB,DWPI	INFLAMMAT$	81333	L4
USPT,PGPB,JPAB,EPAB,DWPI	L1 WITH L2	517	L3
USPT,PGPB,JPAB,EPAB,DWPI	antibod$3	110272	L2
USPT,PGPB,JPAB,EPAB,DWPI	protein adj c	4043	L1

5,147,630 — ~~ay~~ 5,804,392

(FILE 'HOME' ENTERED AT 17:47:47 ON 14 JUL 2001)

FILE 'MEDLINE' ENTERED AT 17:47:54 ON 14 JUL 2001
L1 10122 S PROTEIN(W)C
L2 580623 S ANTIBOD###
L3 832 S L1(P)L2
L4 205370 S INFLAMMA?
L5 41 S L3(P)L4

=> D BIB AB 1-41

L5 ANSWER 1 OF 41 MEDLINE
AN 2001202825 MEDLINE
DN 21125737 PubMed ID: 11054414
TI Lipid oxidation enhances the function of activated protein C.
AU Safa O; Hensley K; Smirnov M D; Esmon C T; Esmon N L
CS Department of Cardiovascular Biology, Oklahoma Medical Research Foundation, University of Oklahoma Health Sciences Center, Oklahoma City 73104, USA.
NC P50 HL54502 (NHLBI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jan 19) 276 (3) 1829-36. Journal code: HIV; 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010417
Last Updated on STN: 20010417
Entered PubMed: 20010306
Entered Medline: 20010412
AB Although lipid oxidation products are usually associated with tissue injury, it is now recognized that they can also contribute to cell activation and elicit anti-◇inflammatory◇ lipid mediators. In this study, we report that membrane phospholipid oxidation can modulate the hemostatic balance. Oxidation of natural phospholipids results in an increased ability of the membrane surface to support the function of the natural anticoagulant, activated ◇protein◇ ◇C◇ (APC), without significantly altering the ability to support thrombin generation. Lipid oxidation also potentiated the ability of protein S to enhance APC-mediated factor Va inactivation. Phosphatidylethanolamine, phosphatidylserine, and polyunsaturation of the fatty acids were all required for the oxidation-dependent enhancement of APC function. A subgroup of thrombotic patients with anti-phospholipid ◇antibodies◇ specifically blocked the oxidation-dependent enhancement of APC function. Since leukocytes are recruited and activated at the thrombus or sites of vessel injury, our findings suggest that after the initial thrombus formation, lipid oxidation can remodel the membrane surface resulting in increased anticoagulant function, thereby reducing the thrombogenicity of the thrombus or injured vessel surface. Anti-phospholipid ◇antibodies◇ that block this process would therefore be expected to contribute to thrombus growth and disease.

L5 ANSWER 2 OF 41 MEDLINE
AN 2001151412 MEDLINE
DN 21115003 PubMed ID: 11236773
TI Efficacy and safety of recombinant human activated protein C for severe sepsis.
CM Comment in: N Engl J Med. 2001 Mar 8;344(10):759-62
AU Bernard G R; Vincent J L; Laterre P F; LaRosa S P; Dhainaut J F; Lopez-Rodriguez A; Steingrub J S; Garber G E; Helterbrand J D; Ely E W; Fisher C J Jr
CS Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232, USA.. gordon.bernard@mcmail.vanderbilt.edu
SO NEW ENGLAND JOURNAL OF MEDICINE, (2001 Mar 8) 344 (10) 699-709. Journal code: NOW; 0255562. ISSN: 0028-4793.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010223
Entered Medline: 20010315
AB BACKGROUND: Drotrecogin alfa (activated), or recombinant human activated ◇protein◇ ◇C◇, has antithrombotic, antiinflammatory, and profibrinolytic properties. In a previous study, drotrecogin alfa activated produced dose-dependent reductions in the levels of markers of coagulation and ◇inflammation◇ in patients with severe sepsis. In this phase 3 trial, we assessed whether treatment with drotrecogin alfa activated reduced the rate of death from any cause among patients with severe sepsis. METHODS: We conducted a randomized, double-blind, placebo-controlled, multicenter trial. Patients with systemic ◇inflammation◇ and organ failure due to acute infection were enrolled and assigned to receive an intravenous infusion of either placebo or drotrecogin alfa activated (24 microg per kilogram of body weight per hour) for a total duration of 96 hours. The prospectively defined primary end point was death from any cause and was assessed 28 days after the start of the infusion. Patients were monitored for adverse events; changes in vital signs, laboratory variables, and the results of microbiologic cultures; and the development of neutralizing ◇antibodies◇ against activated ◇protein◇ ◇C◇. RESULTS: A total of 1690 randomized patients were treated (840 in the placebo group and 850 in the drotrecogin alfa activated group). The mortality rate was 30.8 percent in the placebo group and 24.7 percent in the drotrecogin alfa activated group. On the basis of the prospectively defined primary analysis, treatment with drotrecogin alfa activated was associated with a reduction in the relative risk of death of 19.4 percent (95 percent confidence interval, 6.6 to 30.5) and an absolute reduction in the risk of death of 6.1 percent (P=0.005). The incidence of serious bleeding was higher in the drotrecogin alfa activated group than in the placebo group (3.5 percent vs. 2.0 percent, P=0.06). CONCLUSIONS: Treatment with drotrecogin alfa activated significantly reduces mortality in patients with severe sepsis and may be associated with an increased risk of bleeding.

L5 ANSWER 3 OF 41 MEDLINE
AN 2001051313 MEDLINE
DN 20477812 PubMed ID: 11022125
TI Activated protein C inhibits tumor necrosis factor and macrophage migration inhibitory factor production in monocytes.
AU Schmidt-Supprian M; Murphy C; While B; Lawler M; Kapurniotu A; Voelter W; Smith O; Bernhagen J
CS Laboratory of Biochemistry, Institute for Interfacial Engineering, University of Stuttgart, Nobelstrasse 12, D-70569 Stuttgart, Germany.
SO EUROPEAN CYTOKINE NETWORK, (2000 Sep) 11 (3) 407-13. Journal code: A56. ISSN: 1148-5493.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001212
AB The precise regulatory mechanisms of amplification and downregulation of the pro- and anti-◇inflammatory◇ cytokines in the ◇inflammatory◇ response have not been fully delineated. Although activated ◇protein◇ ◇C◇ (APC) and its precursor ◇protein◇ ◇C◇ (PC) have recently been reported to be promising therapeutic agents in the management of meningococcal sepsis, direct evidence for the anti-◇inflammatory◇ effect remains scarce. We report that APC inhibits in vitro the release of tumor necrosis factor (TNF) and macrophage migration inhibitory factor (MIF), two known cytokine mediators of bacterial septic shock, from lipopolysaccharide (LPS)-stimulated human monocytes. The THP-1 monocytic cell line, when stimulated with LPS and concomitant APC, exhibited a marked reduction in the release of TNF and MIF protein in a concentration-dependent manner compared to cells stimulated with LPS alone. This effect was observed only when incubations were performed in serum-free media, but not in the presence of 1-10% serum. Serum-mediated inhibition could only be overcome by increasing APC concentrations to far beyond physiological levels, suggesting the presence of endogenous serum-derived APC inhibitors. Inhibition of MIF release by APC was found to be independent of TNF, as stimulation of MIF release by LPS was unaltered in the presence of anti-TNF ◇antibodies◇. Our data confirm that the suggested anti-◇inflammatory◇ properties of APC are due to direct inhibition of the release of the pro-◇inflammatory◇ monokine TNF, and imply that the anti-◇inflammatory◇ action of APC is also mediated via inhibition of MIF release.

L5 ANSWER 4 OF 41 MEDLINE
AN 2001037569 MEDLINE
DN 20467158 PubMed ID: 11012640
TI Laboratory findings associated with thrombophilia are not more common in inflammatory bowel disease.
AU Sundaram K K; Cotton R; Hart P; Jones L; Gould S R
CS Department of Gastroenterology, Epsom General Hospital, Epsom, UK.
SO CLINICAL AND LABORATORY HAEMATOLOGY, (2000 Aug) 22 (4) 243-5. Journal code: DKF. ISSN: 0141-9854.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001129
AB Thromboembolic disease (TED) has been recognized as a complication of ◇inflammatory◇ bowel disease (IBD) since the 1930s (Bargen & Barker 1936). The relative contributions of inherited or acquired thrombophilia and the ◇inflammatory◇ response to the mechanism of this tendency is unclear. Thrombotic events are more common in active disease although significant numbers also occur spontaneously, when the disease is in clinical remission (Talbot et al. 1986; Jackson et al. 1997). Studies looking at the prevalence of specific thrombophilic states such as Antithrombin III deficiency (Jackson et al. 1997; Lake, Stauffer & Stuart

1978; Cianco et al. 1996; Ghosh et al. 1983), Factor V Leiden mutation (APC Resistance) (Jackson et al. 1997; Probert et al. 1997; Ardizzone et al. 1998; Liebman et al. 1998), anticardiolipin ◇antibodies◇ (Ciancio et al. 1996), ◇Protein◇ ◇C◇ (Wyshock, Caldwell & Crowley 1988; Korsten & Reis 1992) and Protein S deficiencies (Jorens et al. 1990; Aadland et al. 1992) in IBD have been contradictory or equivocal. We had previously found that IBD patients with a history of TED are not more likely to have a laboratory thrombophilic abnormality than those with uncomplicated disease. We also demonstrated that the prevalence of heterogenous laboratory thrombophilic abnormalities (usually minor) in all IBD patients may be as high as 60%, much higher than the recognized prevalence of TED (Lim, Jones & Gould 1996). We wondered how this would compare with the healthy non-IBD population. We have therefore explored the prevalence of such thrombophilic abnormalities in a group of IBD patients who had no history of TED and compared them with healthy age and sex matched controls.

L5 ANSWER 5 OF 41 MEDLINE
AN 2001037528 MEDLINE
DN 20423371 PubMed ID: 10967662
TI Juvenile cerebral infarction associated with heparin cofactor II abnormality. A case report.
AU Hamasaki S; Motomura M; Nakane S; Nishiura Y; Kondo S
CS First Department of Internal Medicine, Nagasaki University School of Medicine.
SO RINSHO SHINKEIGAKU. CLINICAL NEUROLOGY, (2000 Apr) 40 (4) 402-4.
Journal code: DF2. ISSN: 0009-918X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001124
AB A 15-year-old woman with a history of transient dysarthria two years before, suddenly developed weakness of right upper extremity, right facial palsy, and dysarthria. She was admitted to our hospital on the third day. She had no hypertension, heart murmur and oedema. On neurological examination, she had mild right hemiparesis including face muscles and mild dysarthria. The right knee jerk was brisk with no Babinski's sign. Ataxia and sensory disturbance were not present. T2-weighted MRI showed a hyperintensity at the posterior limb of the left internal capsule. Cerebral angiography was unremarkable. Ultracardiography and 24-hour electrocardiography were normal. Laboratory data revealed no ◇inflammatory◇ findings, liver dysfunction, hyperglycemia and hyperlipidemia. Antinuclear and anticardiolipin ◇antibodies◇ were negative. Prothrombin time was normal, but activated partial thromboplastin time was slightly prolonged (35.4 sec, normal 25.2-34.4). ◇Protein◇ ◇C◇, protein S and antithrombin III were normal. Heparin cofactor II (HC II) activity was decreased (44%) with normal HC II antigen (79%) and so she was diagnosed as heparin cofactor II deficiency type II (heparin cofactor II abnormality). Her father manifesting thromboangitis obliterans also had low HC II activity with normal HC II antigen. However, on her genetic analysis, we didn't detect any mutations in the coding region of HC II gene. Until now she has no recurrence of cerebrovascular attacks. On the basis of these results, we suspect that HC II deficiency was a possible risk factor of cerebral infarction in this case because she was so young and had no general risk factors except for HC II. No stroke associated with HC II deficiency type II has been reported up to date. This case is worth considering etiologies of juvenile cerebral infarction.

L5 ANSWER 6 OF 41 MEDLINE
AN 2001025552 MEDLINE
DN 20391589 PubMed ID: 10937810
TI Further evidence for the presence of anti-protein S autoantibodies in patients with systemic lupus erythematosus.
AU Guermazi S; Regnault V; Gorgi Y; Ayed K; Lecompte T; Dellagi K
CS Laboratoire d'Hematologie, Institut Pasteur de Tunis, Tunis-Belvedere, Tunisia.. sami.guermazi@pasteur.rns.tn
SO BLOOD COAGULATION AND FIBRINOLYSIS, (2000 Jul) 11 (5) 491-8.
Journal code: A5J. ISSN: 0957-5235.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20001108
Entered Medline: 20001116
AB Acquired protein S (PS) deficiency in systemic lupus erythematosus (SLE) has been previously reported, but its mechanism and its possible thrombotic role have not been established. The aim of our study was to provide further evidence for auto-immune PS deficiency in 27 Tunisian SLE patients, using PS-specific enzyme-linked immunosorbent assay (ELISA) and surface plasmon resonance technology (SPR). PS deficiencies for PS activity, free PS or total PS, respectively, were found in 19, 18 and 12 patients. A significant correlation (r= -0.475, P< 0.016) was found between free/total PS ratio and C4bBP levels, suggesting a role of ◇inflammation◇ in free PS deficiency. Immunoglobulin IgG ◇antibodies◇ to PS were detected in four patients by both ELISA and SPR, in six patients only by ELISA, and in two patients only by SPR. Signals for anti-PS IgG by ELISA and SPR were, however, significantly correlated (r = 0.549, P = 0.003). These results suggest that an auto-immune mechanism could account for low PS activity in patients with SLE. Auto-◇antibodies◇ to PS may form immune complexes, inducing increased clearance of PS or interfering with the ◇protein◇ ◇C◇-protein S system.

L5 ANSWER 7 OF 41 MEDLINE
AN 2000451512 MEDLINE
DN 20460266 PubMed ID: 11007200
TI Do new strategies in meningococcemia produce better outcomes?.
AU Leclerc F; Leteurtre S; Cremer R; Fourier C; Sadik A
CS Pediatric Intensive Care Unit, University Hospital of Lille, France.. fleclerc@chru-lille.fr
SO CRITICAL CARE MEDICINE, (2000 Sep) 28 (9 Suppl) S60-3. Ref: 24
Journal code: DTF; 0355501. ISSN: 0090-3493.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200010
ED Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001010
AB Meningococcal septic shock (MSS) has high mortality and morbidity rates. In addition to the traditional prompt antibiotics and respiratory and circulatory support, new treatment strategies have been proposed. AGAINST THE ◇INFLAMMATORY◇ CASCADE: Immunotherapy, such as antiserum to Escherichia coli J5 and human antilipid A monoclonal ◇antibodies◇ /centoxin (HA-1A), did not significantly alter the mortality rate of MSS; we are awaiting the results of the bactericidal/permeability-increasing protein multicenter trial. Two series reported the effects of hemofiltration and hemodiafiltration in MSS, but the true benefits remain unknown. TO TREAT HEMOSTATIC ABNORMALITIES: In MSS, heparin is still controversial and antithrombin concentrate use has been reported in only one child. Several case reports on ◇protein◇ ◇C◇ and recombinant tissue plasminogen activator have been published; the efficacy (improvement in shock and organ dysfunction and reduction in amputation rate) and safety (intracerebral hemorrhage with recombinant tissue plasminogen activator) of these treatments need further evaluation. Blood and plasma exchange appear to be safe and are supposed to reduce mortality, but it is difficult to draw firm conclusions from published studies. Finally, local application of medicinal leeches has been reported to improve purpuric lesions. TO INDUCE VASODILATION: Prostacyclin, or epoprostenol, infusion, sodium nitroprussiate infusion, sympathetic blockade, and topical nitroglycerin have been reported to improve distal perfusion; however, these reports are all anecdotal. OTHER STRATEGIES: Improvement in limb perfusion was achieved after hyperbaric oxygenation in patients with purpura fulminans caused by different pathogens. Most authors recommend monitoring of compartment pressures and performing fasciotomy as indicated. Finally, extracorporeal membrane oxygenation was recently proposed to support seven children with intractable MSS. CONCLUSIONS: There is no proof that unconventional treatments have a significant impact on outcome in MSS; prospective multicenter trials are needed. At present, early recognition of meningococcal sepsis and appropriate treatment seem to be the optimal methods of improving outcome. Efforts to find an effective meningococcal vaccine must be continued.

L5 ANSWER 8 OF 41 MEDLINE
AN 2000439762 MEDLINE
DN 20333314 PubMed ID: 10875131
TI [Epidemiological risk factors for non-traumatic osteonecrosis]. Epidemiologische Risikofaktoren fur die nichttraumatische Osteonekrose.
AU Jones J P
CS Diagnostic Osteonecrosis Center and Research Foundation, Kelseyville, CA 95451, USA.
SO ORTHOPADE, (2000 May) 29 (5) 370-9. Ref: 129
Journal code: OMV; 0331266. ISSN: 0085-4530.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000919
AB Certain fractures and/or dislocations of the femoral head are known to cause arterial injury and result in post-traumatic osteonecrosis. However, the more complex etiology of non-traumatic osteonecrosis is multifactorial and includes chemotherapy, radiotherapy, thermal injuries, and especially coagulopathies, which are now commonly observed in these patients.

Intravascular coagulation with fibrin thrombosis begins in the capillaries and sinusoids of the intraosseous microcirculation, and residual venous thrombosis is more likely to occur if there is coexistent hypofibrinolysis. Coagulopathies are intermediary events, which are always activated by some underlying etiologic risk factor(s). Conditions capable of triggering intravascular coagulation include familial thrombophilia (resistance to activated ◇protein♬ ◇C♬, decreased ◇protein♬ ◇C♬, protein S, or antithrombin III, and hyperhomocystinemia), hyperlipemia and embolic lipid (alcoholism and hypercortisonism), hypersensitivity reactions (allograft organ rejection, immune complexes, and antiphospholipid ◇antibodies♬), bacterial endotoxic (Shwartzman) reactions and various viral infections, proteolytic enzymes (pancreatitis), tissue factor release (◇inflammatory♬ bowel disease, malignancies, neurotrauma, and pregnancy), and other thrombophilic and hypofibrinolytic disorders. Currently known risk factors for non-traumatic osteonecrosis of the femoral head are described briefly in this review article.

L5 ANSWER 9 OF 41 MEDLINE
AN 2000401181 MEDLINE
DN 20304425 PubMed ID: 10843740
TI Production of tumour necrosis factor alpha by primary cultured rat alveolar epithelial cells.
AU McRitchie D I; Isowa N; Edelson J D; Xavier A M; Cai L; Man H Y; Wang Y T;
Keshavjee S H; Slutsky A S; Liu M
CS Departments of Surgery, Medicine, Pediatrics and Pathology, St. Michael's Hospital, Toronto, Ontario, Canada.
SO CYTOKINE, (2000 Jun) 12 (6) 644-54.
Journal code: A52; 9005353. ISSN: 1043-4666.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000823
AB Tumour necrosis factor alpha(TNF-alpha) is one of the most important pro-◇inflammatory♬ cytokines, which plays an important role in host defense and acute ◇inflammation♬ related to tissue injury. The major source of TNF-alpha has been shown to be immune cells such as macrophages and neutrophils. In the present study, we demonstrated that LPS-treatment on alveolar epithelial cells isolated from adult rat lungs also induced a dose- and time-dependent release of TNF-alpha. The purity and identity of these cells were examined by immunofluorescent staining and confocal microscopy with ◇antibodies♬ for cytokeratin and pro-surfactant ◇protein♬ ◇C♬, markers for epithelial cells and type II pneumocytes respectively. Positive staining of TNF-alpha was observed throughout the cell layer and localized intracellularly. LPS-induced TNF-alpha production from alveolar epithelial cells was blocked not only by cycloheximide, an inhibitor of protein translation, but also by actinomycin D, an inhibitor of gene transcription. The mRNA of TNF-alpha rapidly increased within 1 h of LPS stimulation. These data suggest that LPS-induced TNF-alpha production from alveolar epithelial cells is primarily regulated at the transcriptional level, which is different from that of macrophages and neutrophils. TNF-alpha produced by alveolar epithelial cells may function as an alert signal in host defense to induce production of other ◇inflammatory♬ mediators.
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L5 ANSWER 10 OF 41 MEDLINE
AN 2000206021 MEDLINE
DN 20206021 PubMed ID: 10744154
TI Neuroprotection by recombinant thrombomodulin.
AU Taoka Y; Okajima K; Uchiba M; Johno M
CS Department of Laboratory Medicine, Kumamoto University School of Medicine,
Japan.
SO THROMBOSIS AND HAEMOSTASIS, (2000 Mar) 83 (3) 462-8.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000615
AB We examined whether recombinant human soluble thrombomodulin (rhs-TM)
reduces compression trauma-induced spinal cord injury through ◇protein♬ ◇C♬ activation in rats. Administration of rhs-TM, either before or after the induction of spinal cord injury (SCI), markedly reduced the resulting motor disturbances. However, neither rhs-TM pretreated with an anti-rhs-TM monoclonal ◇antibody♬ (MAb) F2H5, which inhibits thrombin binding to rhs-TM, nor those pretreated with MAb R5G12, which selectively inhibits ◇protein♬ ◇C♬ activation by rhs-TM, prevented the motor disturbances. Intramedullary hemorrhages, observed 24 h after trauma, were significantly reduced in animals given rhs-TM. The increase in the tissue levels of tumor necrosis factor-alpha (TNF-alpha), TNF-alpha mRNA expression, and the accumulation of leukocytes in the damaged segment of the spinal cord were significantly inhibited in animals receiving rhs-TM, but these effects were not observed following administration of rhs-TM pretreated with MAb R5G12 or MAb F2H5. Leukocytopenia and activated ◇protein♬ ◇C♬ all produced effects similar to those of rhs-TM. These findings suggest that rhs-TM prevents compression trauma-induced SCI by inhibiting leukocyte accumulation by reducing the expression of TNF-alpha mRNA and such therapeutic effects of rhs-TM could be dependent on its ◇protein♬ ◇C♬ activation capacity. Findings further suggest that thrombomodulin can be implicated not only in the coagulation system but in regulation of the ◇inflammatory♬ response.

L5 ANSWER 11 OF 41 MEDLINE
AN 2000156002 MEDLINE
DN 20156002 PubMed ID: 10688824
TI The endothelial cell protein C receptor aids in host defense against Escherichia coli sepsis.
AU Taylor F B Jr; Stearns-Kurosawa D J; Kurosawa S; Ferrell G; Chang A C; Laszik Z; Kosanke S; Peer G; Esmon C T
CS Oklahoma Medical Research Foundation (OMRF), Oklahoma City 73104, USA..
marie.brewer@omrf.ouhsc.edu
NC 2R01GMHL37704-12 (NIGMS)
P01 HL54804 (NHLBI)
SO BLOOD, (2000 Mar 1) 95 (5) 1680-6.
Journal code: A8G; 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200003
ED Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000329
AB The influence of the endothelial ◇protein♬ ◇C♬ receptor (EPCR) on the host response to Escherichia coli was studied. Animals were treated with 4 separate protocols for survival studies and analysis of physiologic and biochemical parameters: (1) monoclonal ◇antibody♬ (mAb) that blocks ◇protein♬ ◇C♬/activated ◇protein♬ ◇C♬ binding to EPCR plus sublethal numbers of E coli (SLEC) (n = 4); (2) mAb to EPCR that does not block binding plus SLEC (n = 3); (3) SLEC alone (n = 4); and (4) blocking mAB alone (n = 1). Those animals receiving blocking mAb to EPCR plus sublethal E coli died 7 to 54 hours after challenge, whereas all animals treated with the other protocols were permanent survivors. Histopathologic studies of tissues from animals receiving blocking mAb plus SLEC removed at postmortem were compared with those animals receiving SLEC alone killed at T+24 hours. The animals receiving the blocking mAb exhibited consumption of fibrinogen, microvascular thrombosis with hemorrhage of both the adrenal and renal cortex, and an intense influx of neutrophils into the adrenal, renal, and hepatic microvasculature, whereas the tissues from animals receiving only sublethal E coli exhibited none of these abnormal histopathologic changes. Compared with the control animals, the animals receiving the blocking mAb exhibited significantly elevated serum glutamic pyruvic transaminase, anion gap, thrombin-antithrombin complex, IL-6, IL-8, and soluble thrombomodulin. The levels of circulating activated ◇protein♬ ◇C♬ varied too widely to allow a clear determination of whether the extent of ◇protein♬ ◇C♬ activation was altered in vivo by blocking ◇protein♬ ◇C♬ binding to EPCR. We conclude that ◇protein♬ ◇C♬/activated ◇protein♬ ◇C♬ binding to EPCR contributes to the negative regulation of the coagulopathic and ◇inflammatory♬ response to E coli and that EPCR provides an additional critical step in the host defense against E coli. (Blood. 2000;95:1680-1686)

L5 ANSWER 12 OF 41 MEDLINE
AN 2000148238 MEDLINE
DN 20148238 PubMed ID: 10685802
TI Antibodies to thrombomodulin are found in patients with lupus anticoagulant and unexplained thrombosis.
AU Carson C W; Comp P C; Rezaie A R; Esmon N L; Esmon C T
CS Oklahoma Medical Research Foundation, Department of Medicine, College of
Medicine, University of Oklahoma Health Sciences Center, Oklahoma City 73104, USA.
NC HL-30340 (NHLBI)
SO JOURNAL OF RHEUMATOLOGY, (2000 Feb) 27 (2) 384-90.
Journal code: JWX; 7501984. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000404
AB OBJECTIVE: To test the hypothesis that thrombomodulin (TM) may be a target for lupus anticoagulant (LAC) ◇antibodies♬. METHODS: A recombinant soluble form of TM was produced and used as an antigen for an ELISA to detect ◇antibodies♬ to TM (TMAB). Sixty-one samples from 58 patients identified by the coagulation laboratory as having a LAC and 200

patients with unexplained thrombosis were evaluated along with 201 healthy controls. RESULTS: Eighteen (30%) of the 58 patients with a LAC and 20 (10%) of 200 patients with unexplained thrombosis had ◇antibodies◇ to TM. Similar ◇antibodies◇ were found in only 4 (2%) of 201 normal controls. TMAB show selectivity for TM lacking chondroitin sulfate, but do not otherwise have an immunodominant region. The IgG from 6 patients with TMAB was purified, and it bound TM in our ELISA. Three of the 6 IgG fractions inhibited ◇protein◇ ◇C◇ activation 40% to 70% compared to no inhibition in 7 healthy controls. CONCLUSION: Some patients with LAC and unexplained thrombosis have ◇antibodies◇ to TM that may arise in response to TM that has been altered and lost its chondroitin sulfate attachment. ◇Antibodies◇ to TM may be an important risk factor for ◇inflammation◇ and thrombosis in these patients.

L5 ANSWER 13 OF 41 MEDLINE
AN 1999386939 MEDLINE
DN 99386939 PubMed ID: 10455131
TI Purification and characterization of the serum amyloid A3 enhancer factor.
AU Bing Z; Reddy S A; Ren Y; Qin J; Liao W S
CS Department of Biochemistry and Molecular Biology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.
NC AR 38858 (NIAMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Aug 27) 274 (35) 24649-56.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990930
AB Serum amyloid A (SAA) is a major acute-phase protein synthesized and secreted mainly by the liver. In response to acute ◇inflammation◇, its expression may be induced up to 1000-fold, primarily as a result of a 200-fold increase in the rate of SAA gene transcription. We showed previously that cytokine-induced transcription of the SAA3 gene promoter requires a transcriptional enhancer that contains three functional elements: two CCAAT/enhancer-binding ◇protein◇ (◇C◇ /EBP)-binding sites and a third site that interacts with a constitutively expressed transcription factor, SAA3 enhancer factor (SEF). Each of these binding sites as well as cooperation among their binding factors is necessary for maximum transcription activation by ◇inflammatory◇ cytokines. Deletion or site-specific mutations in the SEF-binding site drastically reduced SAA3 promoter activity, strongly suggesting that SEF is important in SAA3 promoter function. To further elucidate its role in the regulation of the SAA3 gene, we purified SEF from HeLa nuclear extracts to near homogeneity by using conventional liquid chromatography and DNA affinity chromatography. Ultraviolet cross-linking and Southwestern experiments indicated that SEF consisted of a single polypeptide with an apparent molecular mass of 65 kDa. Protein sequencing and ◇antibody◇ supershift experiments identified SEF as transcription factor LBP-1c/CP2/LSF. Cotransfection of SEF expression vector with SAA3-luciferase reporter resulted in approximately a 5-fold increase in luciferase activity. Interestingly, interleukin-1 treatment of SEF-transfected cells caused dramatic synergistic activation (31-fold) of the SAA3 promoter. In addition to its role in regulating SAA3 gene expression, we provide evidence that SEF could also bind in a sequence-specific manner to the promoters of the alpha(2)-macroglobulin and Aalpha-fibrinogen genes and to an intronic enhancer of the human Wilm's tumor 1 gene, suggesting a functional role in the regulation of these genes.

L5 ANSWER 14 OF 41 MEDLINE
AN 1999344062 MEDLINE
DN 99344062 PubMed ID: 10415573
TI Factors in xenograft rejection.
AU Robson S C; Schulte am Esch J 2nd; Bach F H
CS Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA.. Srobson@bidmc.harvard.edu
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999 Jun 18) 875 261-76.
Ref: 131
Journal code: 5NM; 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990805
AB Important mechanisms underlying immediate xenograft loss by hyperacute rejection (HAR), in the pig-to-primate combination, have been recently delineated. There are now several proposed therapies that deal with the problem of complement activation and xenoreactive natural ◇antibody◇ (XNA) binding to the vasculature that have been shown to prevent HAR. However, vascularized xenografts are still lost, typically within days, by delayed xenograft rejection (DXR), alternatively known as acute vascular rejection (AVR). This process is characterized by endothelial cell (EC) perturbation, localization of XNA within the graft vasculature, host NK cell and monocyte activation with platelet sequestration and vascular thrombosis. Alternative immunosuppressive strategies, additive anti-complement therapies with the control of any resulting EC activation processes and induction of protective responses have been proposed to ameliorate this pathological process. In addition, several potentially important molecular incompatibilities between activated human coagulation factors and the natural anticoagulants expressed on porcine EC have been noted. Such incompatibilities may be analogous to cross-species alterations in the function of complement regulatory proteins important in HAR. Disordered thromboregulation is potentially relevant to the progression of ◇inflammatory◇ events in DXR and the disseminated intravascular coagulation seen in primate recipients of porcine renal xenografts. We have recently demonstrated the inability of porcine tissue factor pathway inhibitor (TFPI) to adequately neutralize human factor Xa (FXa), the aberrant activation of both human prothrombin and FXa by porcine EC and the failure of the porcine natural anticoagulant, thrombomodulin to bind human thrombin and hence activate human ◇protein◇ ◇C◇. The enhanced potential of porcine von Willebrand factor to associate with human platelet GPIb has been demonstrated to be dependent upon the isolated A1 domain of von Willebrand factor. In addition, the loss of TFPI and vascular ATPDase/CD39 activity following EC activation responses would potentiate any procoagulant changes within the xenograft. These developments could exacerbate vascular damage from whatever cause and enhance the activation of platelets and coagulation pathways within xenografts resulting in graft infarction and loss. Analysis of these and the other putative factors underlying DXR should lead to the development and testing of genetic approaches that, in conjunction with selected pharmacological means, may further prolong xenograft survival to a clinically relevant extent.

L5 ANSWER 15 OF 41 MEDLINE
AN 1999262503 MEDLINE
DN 99262503 PubMed ID: 10329925
TI Antithrombin replacement in patients with sepsis and septic shock.
AU Giudici D; Baudo F; Palareti G; Ravizza A; Ridolfi L; D' Angelo A
CS Unita di Terapia Intensiva, IRCCS H S.Raffaele, Milan.
SO HAEMATOLOGICA, (1999 May) 84 (5) 452-60. Ref: 54
Journal code: FYB; 0417435. ISSN: 0390-6078.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990803
AB Sepsis is a frequent complication of critically ill patients and its incidence is increasing. Currently, septic shock is the most common cause of death in non-coronary intensive care units. Over the last 10 to 15 years, new antibiotics and increasingly sophisticated critical care have had little impact on the mortality rate of septic shock. The Italian SEPSIS Study, carried out in 99 intensive care units in 1994, reported mortality rates of 52% and 82% for severe sepsis and septic shock respectively. New therapeutic approaches aimed at neutralizing microbial toxins and modulating host mediators have shown some efficacy in large clinical trials and/or in animal models, but to date, no therapy of sepsis aimed at reversing the effects of bacterial toxins or of harmful endogenous mediators of ◇inflammation◇ has gained widespread clinical acceptance. Because of the strong association of severe sepsis with a state of activation of blood coagulation and of the potential role of capillary thrombosis in the development of the multiple organ dysfunction syndrome, anticoagulant agents have been tested in the setting of septic shock. However, neither administration of heparin nor of active site-blocked factor Xa or of anti-tissue factor ◇antibodies◇ have proven effective in preventing deaths due to septic shock in animal models. In contrast, infusion of antithrombin, ◇protein◇ ◇C◇ , or tissue factor pathway inhibitor all resulted in a significant survival advantage in animals receiving lethal doses of E. Coli. Antithrombin concentrates have been used in a significant number of critically ill patients. A double-blind, placebo controlled study carried out in 3 italian intensive care units has recently shown that the administration of antithrombin aimed to normalize plasma antithrombin activity had a net beneficial effect on 30-day survival of patients requiring respiratory and/or hemodynamic support because of severe sepsis and/or post-surgery complications.

L5 ANSWER 16 OF 41 MEDLINE
AN 1999250412 MEDLINE
DN 99250412 PubMed ID: 10233774
TI Removal of stem cell factor or addition of monoclonal anti-c-KIT antibody induces apoptosis in murine melanocyte precursors.
AU Ito M; Kawa Y; Ono H; Okura M; Baba T; Kubota Y; Nishikawa S I; Mizoguchi M
CS Department of Dermatology, St. Marianna University School of Medicine, Kawasaki, Japan.
SO JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1999 May) 112 (5)

796-801.
Journal code: IHZ; 0426720. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990712
Last Updated on STN: 20000303
Entered Medline: 19990618
AB Previous findings indicate that the ◊protein◊ ◊c◊-KIT and its ligand, stem cell factor (SCF) play a crucial role in the development of melanocytes from their precursors in the embryonic neural crest cells. Using a monoclonal anti-c-KIT ◊antibody◊, ACK2, which is an antagonistic blocker of c-KIT function, we and colleagues demonstrated that mouse melanocytes disappeared with the injection of ACK2 during certain periods of embryonic and postnatal life. The precise mechanisms of this disappearance, however, remain unclear. Because melanocytes disappeared without any ◊inflammation◊ in these in vivo studies, we suspect that apoptosis was a main cause of their disappearance. In this study, to clarify the underlying mechanism, we studied whether ACK2 induces apoptosis in c-KIT-positive melanoblasts, which appear in mouse neural crest cells cultured with SCF from 9.5 d old mouse embryos. With an in situ apoptosis detection kit, a significant increase in apoptosis was detected after the removal of SCF, which further increased with the addition of ACK2 during SCF-dependent periods. The occurrence of apoptosis in the cultured cells was also demonstrated by a DNA analysis and electron microscopy. Immunohistochemical double staining confirmed that the apoptotic cells were c-KIT positive, and the electron microscopy showed that these apoptotic cells were melanocyte precursors. It was therefore demonstrated that apoptosis was induced in the SCF-dependent c-KIT-positive melanocytes in vitro when the SCF/c-KIT interaction was obstructed. These findings elucidate the mechanism of the regulation of melanocyte development, and the survival and proliferation of these precursor cells, by SCF/c-KIT interaction.

L5 ANSWER 17 OF 41 MEDLINE
AN 1999183956 MEDLINE
DN 99183956 PubMed ID: 10084210
TI Coagulopathies and osteonecrosis.
AU Jones J P Jr
CS Diagnostic Osteonecrosis Center and Research Foundation, Kelseyville, California 95451, USA.
SO ACTA ORTHOPAEDICA BELGICA, (1999) 65 Suppl 1 5-8. Ref: 24
Journal code: 1G2; 2985165R. ISSN: 0001-6462.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990414
AB Intravascular coagulation of the intraosseous microcirculation (capillaries and venous sinusoids) progressing to generalized venous thrombosis, and less commonly retrograde arterial occlusion, now appears to be the cause of nontraumatic osteonecrosis. However, this coagulopathy is only an intermediary event, which is always activated by some underlying etiologic risk factor(s). Conditions capable of triggering intravascular coagulation include familial thrombophilia (resistance to activated ◊protein◊ ◊C◊, decreased ◊protein◊ ◊C◊, protein S, or antithrombin III), hyperlipemia and embolic lipid (alcoholism and hypercortisonism), hypersensitivity reactions (allograft organ rejection, immune complexes, and antiphospholipid ◊antibodies◊), bacterial endotoxic (Shwartzman) reactions and various viral infections, proteolytic enzymes (pancreatitis), tissue factor release (◊inflammatory◊ bowel disease, malignancies, neurotrauma, and pregnancy), and other prothrombotic and hypofibrinolytic conditions.

L5 ANSWER 18 OF 41 MEDLINE
AN 1999117325 MEDLINE
DN 99117325 PubMed ID: 9918531
TI Regulation of CCAAT/Enhancer binding protein, interleukin-6, interleukin-6 receptor, and gp130 expression during myocardial ischemia/reperfusion.
CM Comment in: Circulation. 2000 May 9;101(18):E194
AU Chandrasekar B; Mitchell D H; Colston J T; Freeman G L
CS Division of Cardiology, University of Texas Health Science Center and South Texas Veterans Health Care System, Audie L. Murphy Division, San Antonio, Tex 78284-7872, USA.
SO CIRCULATION, (1999 Jan 26) 99 (3) 427-33.
Journal code: DAW; 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199902
ED Entered STN: 19990223
Last Updated on STN: 20000616
Entered Medline: 19990211
AB BACKGROUND: Interleukin (IL)-6 is elevated in myocardium after ischemia and reperfusion. The IL-6 promoter/enhancer region contains response elements for nuclear factor-kappaB, AP-1, and CCAAT/enhancer binding ◊protein◊ (◊C◊/EBP). Expression and regulation of C/EBP in rat myocardium after ischemia and reperfusion has not been defined, nor has the behavior of the specific IL-6 receptor (IL-6R) or the signal transducer gp130. METHODS AND RESULTS: C/EBP DNA binding activity was not detected in shams or in previously ischemic tissue at 15 minutes of reperfusion; it was detected at 30 minutes of reperfusion, increased at 1 hour of reperfusion, and declined by 6 hours of reperfusion. A supershift was observed with anti-C/EBP-beta but not with anti-alpha or anti-delta ◊antibodies◊. mRNA and protein levels of IL-6 and gp130 were detected at low levels in controls, increased at 1 hour of reperfusion, and remained high until 6 hours of reperfusion. IL-6R mRNA and protein were not detected in controls, but its mRNA was induced at 1 hour of reperfusion and its protein at 2 hours of reperfusion. Although effects of reperfusion were rapid, in ischemic tissue not reperfused, low levels of C/EBP were detected at 4 hours, and at 24 hours the levels were slightly elevated. Significant upregulation in IL-6, IL-6R, and gp130 occurred only at 24 hours of sustained ischemia. CONCLUSIONS: Reperfusion after a brief period of ischemia caused induction of myocardial C/EBP (beta-subunit). The rapid and sustained production of IL-6 with concomitant expression of IL-6 receptor and gp130 suggest that these factors may participate in a local ◊inflammatory◊ cascade after myocardial ischemia and reperfusion.

L5 ANSWER 19 OF 41 MEDLINE
AN 1999032336 MEDLINE
DN 99032336 PubMed ID: 9812085
TI Atherogenic, hemostatic, and other potential risk markers in subjects with previous isolated myocardial infarction compared with long-standing uncomplicated stable angina.
AU Bogaty P; Robitaille N M; Solymoss S; Boyer L; Auger D; Labbe L; Simard S; Rail J; Genest J Jr; Turgeon J
CS Quebec Heart Institute/Laval Hospital, Laval University, Ste-Foy, Canada.
SO AMERICAN HEART JOURNAL, (1998 Nov) 136 (5) 884-93.
Journal code: 3BW; 0370465. ISSN: 0002-8703.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981202
AB BACKGROUND: Several atherogenic, hemostatic, ◊inflammatory◊, and genetic parameters and markers have been implicated as risk factors in coronary artery disease, although whether they are risk factors for acute as opposed to chronic coronary disease is unclear. METHODS AND RESULTS: Fifty subjects with an isolated myocardial infarction >3 months previously were compared with 50 subjects with a minimum 3-year history of stable angina, documented coronary artery disease, normal electrocardiogram and normal ventricular wall motion, and no episode suggesting infarction or unstable angina. Biologic variables analyzed included apolipoprotein B (apo B), lipoprotein (a), C-reactive protein (CRP), fibrinogen, factor VII, tissue plasminogen activator (TPA) and inhibitor (PAI-1), thrombin-antithrombin (TAT), fragment 1+2 (F1+2), von Willebrand factor (vWF), activated ◊protein◊ ◊C◊ resistance, homocyst(e)ine, anticardiolipin ◊antibodies◊, blood group, and the angiotensin-converting enzyme insertion/deletion (I/D) and angiotensin II receptor gene polymorphisms. There were no significant differences between the 2 groups for any of the variables studied, although fibrinogen and F 1+2 tended to be slightly higher in the angina group (P = .09 for each). These significant correlations were present: age with fibrinogen, homocyst(e)ine, and vWF; factor VII with apo B, homocyst(e)ine, and TPA; apo B with TPA and CRP; CRP with fibrinogen, TPA, PAI-1, and factor VII; fibrinogen with vWF. CONCLUSIONS: Examination of atherogenic, hemostatic, ◊inflammation◊, and genetic variables in the clinically quiescent state permitted no distinction between subjects with a previous isolated myocardial infarction in contrast to those with long-standing uncomplicated stable angina, favoring the notion that acute coronary events occur at random on a varying background of atherosclerosis. The multiple correlations found among these variables also underscore their complex interaction in the atherosclerotic process.

L5 ANSWER 20 OF 41 MEDLINE
AN 1998100487 MEDLINE
DN 98100487 PubMed ID: 9437833
TI Harbor seal (Phoca vitulina) C-reactive protein (C-RP): purification, characterization of specific monoclonal antibodies and development of an immuno-assay to measure serum C-RP concentrations.
AU Funke C; King D P; Brotheridge R M; Adelung D; Stott J L
CS Marine Mammal Center, Marin Headlands, GGNRA, Sausalito, CA 94965, USA.
SO VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1997 Oct 6) 59 (1-2) 151-62.
Journal code: XCB; 8002006. ISSN: 0165-2427.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199802
ED Entered STN: 19980224
Last Updated on STN: 19980224
Entered Medline: 19980212
AB C-reactive ◇protein/◇ (◇C/◇-RP) was purified from harbor seal (Phoca vitulina) serum by calcium dependant phosphoryl-choline and protein A affinity chromatography. Polyacrylamide gel electrophoresis under reducing conditions revealed a single protein moiety with a molecular weight of approximately 25 kDa. An internal peptide derived from this purified protein was subjected to N-terminal amino acid sequencing. A high amino acid sequence similarity was obtained with other published mammalian C-RP molecules confirming that the purified protein was a C-RP homologue. Eight specific monoclonal ◇antibodies/◇ (P13, P51, P87, P101, P106, P130, P157 and P219) were raised against this purified protein. All 8 monoclonal ◇antibodies/◇ immunoblotted with the 25 kDa C-RP subunit under reducing conditions. A competitive immunoassay was developed identifying elevated C-RP concentrations in harbor seal serum samples with clinical evidence of ◇inflammatory/◇ disease. Application of this immunoassay for the measurement C-RP may provide valuable information for the clinical assessment of harbor seal health.

L5 ANSWER 21 OF 41 MEDLINE
AN 97433191 MEDLINE
DN 97433191 PubMed ID: 9288860
TI Is the loss of endothelial thrombomodulin involved in the mechanism of chronicity in late radiation enteropathy?.
AU Richter K K; Fink L M; Hughes B M; Sung C C; Hauer-Jensen M
CS Department of Surgery, University of Arkansas for Medical Sciences and John L. McClellan VAMC, Little Rock 72205, USA.
SO RADIOTHERAPY AND ONCOLOGY, (1997 Jul) 44 (1) 65-71.
Journal code: RAE; 8407192. ISSN: 0167-8140.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971021
Last Updated on STN: 19971021
Entered Medline: 19971009
AB BACKGROUND AND PURPOSE: Radiation enteropathy is characterized by locally elevated levels of ◇inflammatory/◇ and fibrogenic cytokines. Microvascular injury may sustain these alterations through persistent local hypercoagulopathy, platelet aggregation, leukocyte adhesion and release of biologically active mediators. This study assessed the relationship of endothelial thrombomodulin (TM), a key regulator of the ◇protein/◇ ◇C/◇ anticoagulant pathway and marker of endothelial function, with transforming growth factor beta (TGF-beta) immunoreactivity and morphologic alterations in radiation enteropathy. MATERIALS AND METHODS: Small bowel resection specimens from 9 patients with radiation enteropathy were analyzed by computerized quantitative immunohistochemistry using ◇antibodies/◇ against TM, von Willebrand factor (vWF) and TGF-beta. Identical measurements were performed on intestinal resection specimens from otherwise healthy penetrating trauma victims and on archived small intestines. A previously validated image analysis technique was used to assess submucosal vessels for TM and vWF immunoreactivity, and the intestinal wall for total extracellular matrix-associated TGF-beta immunoreactivity. RESULTS: Specimens from irradiated patients showed prominent submucosal and subserosal thickening and fibrosis, and obliterative vasculopathy. Control specimens were histopathologically normal. Vascular density and vWF immunoreactivity were similar in radiation enteropathy patients and controls. The image-analysis techniques were highly reproducible, with correlation coefficients for repeated measurements ranging from 0.86 to 0.93. Radiation enteropathy specimens exhibited a highly significant reduction in the number and proportion of TM-positive submucosal vessels per unit area ($P < 0.0001$) and increased intestinal wall TGF-beta immunoreactivity ($P = 0.002$). CONCLUSIONS: These data support the theory that sustained endothelial dysfunction is involved in the molecular pathogenesis of radiation enteropathy, and point to TM as important in the chronic nature of radiation enteropathy and a potential target for prophylactic and therapeutic interventions.

L5 ANSWER 22 OF 41 MEDLINE
AN 97385725 MEDLINE
DN 97385725 PubMed ID: 9241739
TI Respective evaluation of the prevalence of haemostasis abnormalities in unexplained primary early recurrent miscarriages. The Nimes Obstetricians and Haematologists (NOHA) Study.
AU Gris J C; Ripart-Neveu S; Maugard C; Tailland M L; Brun S; Courtieu C; Biron C; Hoffet M; Hedon B; Mares P
CS Consultations et Laboratoire d'Hematologie, CHU, Nimes, France.
SO THROMBOSIS AND HAEMOSTASIS, (1997 Jun) 77 (6) 1096-103.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970922
Last Updated on STN: 19980206
Entered Medline: 19970911
AB The prevalence of haemostasis abnormalities was evaluated in 500 consecutive women with unexplained primary recurrent miscarriages. Two matched reference groups with no antecedent of miscarriage were studied: 100 healthy mothers and 50 childless women. In the prospective part of the study, we found 9.4% of the patients (95% C.I.: 6.8-12%) with an isolated factor XII deficiency, 7.4% of the patients (5.0-9.8%) with primary antiphopholipid ◇antibodies/◇, 47% of the patients (42.6-51.4%) with an insufficient response to the venous occlusion test and an isolated hypofibrinolysis was found in 42.6% (38.2-47%) of the patients (reference groups: respectively 0/150, 3/150, 2/150, $p < 10(-3)$). Willebrand disease, fibrinogen, deficiency, antithrombin, ◇protein/◇ ◇C/◇ or protein S deficiencies were not more frequent in recurrent aborters than in members of the reference groups. In the retrospective part of the study, cases of plasma resistance to activated ◇protein/◇ ◇C/◇ were not abnormally frequent. Patients had higher Willebrand factor antigen (vWF), tissue-type plasminogen activator antigen (t-PA), plasminogen activator inhibitor activity (PAI) and D-dimers (D-Di) than the reference women. Values of vWF, t-PA, PAI and D-Di were altogether correlated but were not related to C-reactive protein concentrations. Among patients, those with an antiphospholipid syndrome and those with an insufficient response to the venous occlusion test had higher vWF, t-PA, PAI and D-Di values than the patients with none of the haemostasis-related abnormalities. Thus, factor XII deficiency and hypofibrinolysis (mainly high PAI) are the most frequent haemostasis-related abnormalities found in unexplained primary recurrent aborters. In patients with antiphospholipid ◇antibodies/◇ or hypofibrinolysis, there is a non-◇inflammatory/◇ ongoing chronic elevation of markers of endothelial stimulation associated with coagulation activation. This should allow to define subgroups of patients for future therapeutic trials.

L5 ANSWER 23 OF 41 MEDLINE
AN 97318288 MEDLINE
DN 97318288 PubMed ID: 9175241
TI Protein S deficiency and antibodies to protein S in patients with Behcet's disease.
AU Guermazi S; Hamza M; Dellagi K
CS Laboratoire d'Hematologie, Institut Pasteur de Tunis, Tunisie.
SO THROMBOSIS RESEARCH, (1997 May 1) 86 (3) 197-204.
Journal code: VRN; 0326377. ISSN: 0049-3848.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
ED Entered STN: 19970825
Last Updated on STN: 19970825
Entered Medline: 19970812
AB Thrombosis occurs in 20 to 30% of patients with Behcet's disease (BD). Most of the reported hemostatic abnormalities are related to the ◇inflammatory/◇ syndrome. We have assessed the activity of antithrombin III, ◇protein/◇ ◇C/◇ and protein S (PS), in 30 patients with BD and in 30 healthy controls. Thrombosis antecedents were found in 16 patients. Antithrombin III and ◇protein/◇ ◇C/◇ were within the normal range, however free PS and PSactivity were significantly decreased in patients as compared to control group. PS deficiency detected in eight patients, was associated to thrombosis in 6 of them. No correlation was found between free PS/total PS ratio and C4bBP levels. ◇Antibodies/◇ to PS were screened by ELISA and were present in 6 patients, associated to PS deficiency in 4, and to thrombosis antecedents in 5 cases. PS deficiency was transient in two patients, associated to a persistent antiPS in one of them. These findings suggest that auto-immune acquired PS deficiency may be involved in the pathogenesis of thrombotic events in BD.

L5 ANSWER 24 OF 41 MEDLINE
AN 97247468 MEDLINE
DN 97247468 PubMed ID: 9093595
TI Thrombosis in inflammatory bowel disease: clinical setting, procoagulant profile and factor V Leiden.
AU Jackson L M; O'Gorman P J; O'Connell J; Cronin C C; Cotter K P; Shanahan F
CS Department of Medicine, National University of Ireland, Cork, Ireland.
SO QJM, (1997 Mar) 90 (3) 183-8.
Journal code: B4V; 9438285. ISSN: 1460-2725.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970424
Last Updated on STN: 20000303
Entered Medline: 19970417
AB Patients with ◇inflammatory/◇ bowel disease have an increased frequency of thromboembolism, and microvascular thrombosis has been proposed as a contributory pathogenic factor. The mechanism of enhanced procoagulant activity is not understood. We examined the clinical setting of thromboembolic events in 52 patients with Crohn's disease or ulcerative colitis, and assessed the procoagulant laboratory profile, including Factor V Leiden, in a subset of 20 patients to identify procoagulant risk factors. Patients who developed thrombosis tended to be young; 60% of thrombotic events occurred in patients under 50 years. Multiple

thromboembolic episodes occurred in 13% and unusual sites of thrombosis (e.g. intracardiac, cerebral, inominate veins) in 11%. No risk factor was identifiable in 52% of cases and two-thirds of thromboses occurred in an out-patient setting. The mortality rate was 8%. Evidence for ◇inflammatory/◇ disease activity was found in only 45% of patients with ulcerative colitis at the time of the thromboembolic event, in contrast to 89% of those with Crohn's disease. Assays for specific coagulation defects were negative in all cases tested (protein S, C were normal in 17/17; anti-thrombin III, anti-phospholipid ◇antibodies/◇ and activated ◇protein/◇ ◇C/◇ resistance were negative in 20/20, and only 1/20 patients was found to be heterozygous for Factor V leiden. Thrombosis in ◇inflammatory/◇ bowel disease is important because it occurs in a young population, often in unusual sites, and has a high mortality. The development of thrombosis is related to active ◇inflammatory/◇ disease in most patients with Crohn's disease but apparently not in those with ulcerative colitis. Since approximately half of the patients had no other identifiable risk factor, there remains a substantial group of patients with IBD who develop thrombosis for unknown reasons.

L5 ANSWER 25 OF 41 MEDLINE
AN 97244307 MEDLINE
DN 97244307 PubMed ID: 9125256
TI Low-level increases in serum C-reactive protein are present in early osteoarthritis of the knee and predict progressive disease.
AU Spector T D; Hart D J; Nandra D; Doyle D V; Mackillop N; Gallimore J R; Pepys M B
CS Whipps Cross Hospital, London, UK.
SO ARTHRITIS AND RHEUMATISM, (1997 Apr) 40 (4) 723-7.
Journal code: 90M; 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199704
ED Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970424
AB OBJECTIVE:To examine the role of low-grade ◇inflammation/◇ in the etiology and progression of early osteoarthritis (OA) of the knee. METHODS: We used a new, high-sensitivity, automated monoclonal ◇antibody/◇ immunoassay for the classic acute-phase ◇protein/◇ , ◇C/◇-reactive protein (CRP), in serum. Anteroposterior radiographs of the knee with weight bearing were obtained on 845 women (ages 44-67) on entry into a population-based study of OA in Chingford, North London. In those defined radiologically as "cases," the knee radiographs were repeated after 4 years. RESULTS: Levels of CRP were higher in 105 women with knee OA defined radiologically as Kellgren-Lawrence grade 2+ (median 2.4 mg/liter, interquartile range [IQR] 1.0-5.1), compared with 740 women without OA (median 0.7 mg/liter, IQR 0.3-1.8) (P < 0.001). Median levels of CRP were higher in the 31 women whose disease progressed at least 1 Kellgren-Lawrence grade (median 2.6 mg/liter, IQR 1.9-4.6), compared with the 39 whose disease did not (median 1.3 mg/liter, IQR 0.6-2.4) (P = 0.006) . The significance of these differences persisted after adjustment for age, weight, height, smoking, knee pain, or injury. Classifying disease by the presence of joint space narrowing or osteophytes alone produced similar results. CONCLUSION: CRP
levels are modestly but significantly increased in women with early knee OA, and higher levels predict those whose disease will progress over 4 years, suggesting that low-grade ◇inflammation/◇ may be a significant aspect of early OA and may be amenable to therapeutic intervention and secondary prevention.

L5 ANSWER 26 OF 41 MEDLINE
AN 97184462 MEDLINE
DN 97184462 PubMed ID: 9032264
TI Cloning of the novel human myeloid-cell-specific C/EBP-epsilon transcription factor.
AU Chumakov A M; Grillier I; Chumakova E; Chih D; Slater J; Koeffler H P
CS Department of Medicine, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, California 90048, USA.
NC CA42710 (NCI)
DK41936 (NIDDK)
DK42792 (NIDDK)
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Mar) 17 (3) 1375-86.
Journal code: NGY; 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U80982
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19990129
Entered Medline: 19970314
AB Chicken NF-M transcription factor, in cooperation with either c-Myb or v-Myb, is active in the combinatorial activation of myeloid-cell-specific genes in heterologous cell types, such as embryonic fibroblasts. In humans, similar effects were observed with homologous members of the CCAAT/enhancer-binding ◇protein/◇ (◇C/◇/EBP) family of transcriptional regulators, especially the human homolog of chicken NF-M, C/EBP-beta (NF-IL6). However, the NF-IL6 gene is expressed in a variety of nonmyeloid cell types and is strongly inducible in response to ◇inflammatory/◇ stimuli, making it an unlikely candidate to have an exclusive role as a combinatorial differentiation switch during myelopoiesis in human cells. By using a reverse transcription-PCR-based approach and a set of primers specific for the DNA-binding domains of highly homologous members of the C/EBP family of transcriptional regulators, we have cloned a novel human gene encoding a member of the C/EBP gene family, identified as the human homolog of CRP1, C/EBP-epsilon.
A 1.2-kb cDNA encoding full-length human C/EBP-epsilon was cloned from a promyelocyte-late myeloblast-derived lambda gt11 library. Molecular analysis of the cDNA and genomic clones indicated the presence of two exons encoding a protein with an apparent molecular mass of 32 kDa and a pI of 9.5. Primer extension analysis of C/EBP-epsilon mRNA detected a single major transcription start site approximately 200 bp upstream of the start codon. The putative promoter area is similar to those of several other myeloid-cell-specific genes in that it contains no TATAAA box but has a number of purine-rich stretches with multiple sites for the factors of the Ets family of transcriptional regulators. Northern blot analyses indicated a highly restricted mRNA expression pattern, with the strongest expression occurring in promyelocyte and late-myeloblast-like cell lines. Western blot and immunoprecipitation studies using rabbit anti-C/EBP-epsilon ◇antibodies/◇ raised against the N-terminal portion of C/EBP-epsilon (amino acids 1 to 115) showed that C/EBP-epsilon is a 32-kDa nuclear phosphoprotein. The human C/EBP-epsilon protein exhibited strong and specific binding to double-stranded DNA containing consensus C/EBP sites. Cotransfection of the C/EBP-epsilon sense and antisense expression constructs together with chloramphenicol acetyltransferase reporter vectors containing myeloid-cell-specific c-mim and human myeloperoxidase promoters suggested a role for C/EBP-epsilon transcription factor in the regulation of a subset of myeloid-cell-specific genes. Transient tranfection of a promyelocyte cell line (NB4) with a C/EBP-epsilon expression plasmid increased cell growth by sevenfold, while antisense C/EBP-epsilon caused a fivefold decrease in clonal growth of these cells.

L5 ANSWER 27 OF 41 MEDLINE
AN 97054509 MEDLINE
DN 97054509 PubMed ID: 8898806
TI Impairments of the protein C system and fibrinolysis in infection-associated stroke.
AU Macko R F; Ameriso S F; Gruber A; Griffin J H; Fernandez J A; Barndt R; Quismorio F P Jr; Weiner J M; Fisher M
CS Department of Neurology, University of Southern California School of Medicine, Los Angeles 90033, USA.
NC HL-15722 (NHLBI)
NS-20989 (NINDS)
P01NS31945 (NINDS)
+
SO STROKE, (1996 Nov) 27 (11) 2005-11.
Journal code: V2J; 0235266. ISSN: 0039-2499.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205
AB BACKGROUND AND PURPOSE: Infection/◇inflammation/◇ appears to be an important predisposing risk factor for brain infarction, but little is known regarding underlying molecular mechanisms. We examined the hypothesis that patients with brain infarction preceded by infection/ ◇inflammation/◇ within 1 week could be identified by a distinctive procoagulant laboratory profile characterized by abnormalities in the ◇protein/◇ ◇C/◇ system and endogenous fibrinolysis. METHODS: We performed a case-control study examining the relationship between preceding systemic infectious/◇inflammatory/◇ syndromes and selected immunohematologic variables in 36 patients with acute brain infarction and 81 control subjects (community control subjects [n = 47] and hospitalized nonstroke neurological patient controls [n = 34]). RESULTS: The stroke group had a lower mean level of the circulating antithrombotic enzyme activated ◇protein/◇ ◇C/◇ (APC) (4.33 +/- 0.34% [log-transformed percentage of control value, mean +/- SD]) than community control subjects (4.51 +/- 0.27%, P < .02) or hospitalized neurological patient controls (4.57 +/- 0.31%, P < .005). The lowest circulating APC levels were found in the stroke group with antecedent infection/◇inflammation/◇ within 1 week preceding index brain infarction (4.23 +/- 0.4%, n = 12). Within the stroke group, circulating APC levels were inversely related to IgG isotype anticardiolipin ◇antibody/◇ titers (r = -.55, P < .001). Only the stroke group with infection/◇inflammation/◇ within 1 week had elevated plasma C4b binding protein compared with control subjects (141 +/- 61% versus 112 +/- 44%, P < .05). Stroke patients with antecedent infection/ ◇inflammation/◇ had a distinctively lower ratio of active tissue plasminogen activator to plasminogen activator inhibitor (0.11 +/- 0.04, n = 9) than other stroke patients (0.19 +/- 0.06, n = 9, P < .01) and control subjects (0.22 +/- 0.16, n = 17, P < .02). CONCLUSIONS: Impairments in the ◇protein/◇ ◇C/◇ pathway and endogenous fibrinolysis may contribute to the increased risk for brain infarction after recent (< or = 1 week) infection/◇inflammation/◇. A decrease in the circulating anticoagulant APC may be related to elevated

antiphospholipid ◇antibody◇ titers.

L5 ANSWER 28 OF 41 MEDLINE
AN 97012964 MEDLINE
DN 97012964 PubMed ID: 9163067
TI Hemostatic abnormalities in inflammatory bowel disease.
AU Chiarantini E; Valanzano R; Liotta A A; Cellai A P; Fedi S; Ilari I; Prisco D; Tonelli F; Abbate R
CS Istituto di Clinica Medica Generale e Cardiologia, Unita di Chirurgia Generale, University of Florence, Italy.
SO THROMBOSIS RESEARCH, (1996 Apr 15) 82 (2) 137-46.
Journal code: VRN; 0326377. ISSN: 0049-3848.
CY United States
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970527
AB Patients affected by ◇inflammatory◇ bowel disease (IBD) frequently suffer from thromboembolic events. Aims of this study were to investigate hemostatic system and the presence of antiphospholipid ◇antibodies◇ (aPL) in IBD patients. Forty-one patients affected by Crohn's disease (CD) and 19 by ulcerative colitis (UC) were studied, compared to 40 healthy control subjects. Platelet count (PLT), PT, aPTT, fibrinogen (Fib), prothrombin fragment F1+2, antithrombin (AT), ◇protein◇ ◇C◇ (PC), protein S (PS), factor XIII (FXIII), plasminogen (PLG), plasminogen activator inhibitor (PA1), spontaneous platelet aggregation in platelet-rich plasma (PRP-SPA) and in whole blood (WB-SPA), and antiphospholipid ◇antibodies◇ (aPL) were evaluated. PLT, Fib, F1+2 and WB-SPA were significantly increased in IBD patients (p at least <0.05) both in active and inactive phases; aPL positivity was more frequent (p<0.05) and FXIII was significantly decreased (p<0.05) in comparison to control subjects. The thrombophilic state of IBD patients is not related to the degree of activity of the disease or to previous thrombotic events; aPL express the immunological alterations connected with IBD and are not the main cause of thrombotic events.

L5 ANSWER 29 OF 41 MEDLINE
AN 96362515 MEDLINE
DN 96362515 PubMed ID: 8742656
TI Antiphospholipid syndrome manifested by ischemic stroke in a patient with Crohn's disease.
AU Mevorach D; Goldberg Y; Gomori J M; Rachmilewitz D
CS Department of Medicine, Hebrew University, Jerusalem, Israel.
SO JOURNAL OF CLINICAL GASTROENTEROLOGY, (1996 Mar) 22 (2) 141-3.
Journal code: IBG; 7910017. ISSN: 0192-0790.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 20000303
Entered Medline: 19961021
AB Cerebrovascular accidents are rare but well documented in patients with Crohn's disease. Up to 10% of hypercoagulable state manifestations reported in association with ◇inflammatory◇ bowel disease are ischemic strokes. However, no clear mediating factor has thus far been suggested. A 44-year-old woman with Crohn's disease for 25 years developed
a left temporal stroke associated with anticardiolipin ◇antibody◇ and lupus anticoagulant suggesting antiphospholipid syndrome. A thorough evaluation did not reveal any other risk factor for ischemic stroke. No possible sources of emboli were found in the carotids and heart, and no deficiencies of ◇protein◇ ◇C◇ and activated ◇protein◇ ◇C◇, protein S, and anti-thrombin III leading to hypercoagulable state were present. There may be a possible association between antiphospholipid syndrome and hypercoagulable state in Crohn's disease.

L5 ANSWER 30 OF 41 MEDLINE
AN 96302769 MEDLINE
DN 96302769 PubMed ID: 8743182
TI Infusion of phospholipid vesicles amplifies the local thrombotic response to TNF and anti-protein C into a consumptive response.
AU Taylor F B Jr; He S E; Chang A C; Box J; Ferrell G; Lee D; Lockhart M; Peer G; Esmon C T
CS Oklahoma Medical Research Foundation, Oklahoma City 73104, USA.
NC 2R01 GM37704 (NIGMS)
R37 HL30340 (NHLBI)
SO THROMBOSIS AND HAEMOSTASIS, (1996 Apr) 75 (4) 578-84.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961105
AB ◇Inflammation◇ often is considered a contributing factor to both thrombosis and disseminated intravascular coagulation. The molecular mechanisms that dictate which of these clinical manifestations will result from the ◇inflammatory◇ stimulus remain obscure. Bacterial infection and certain tumors are common initiators of the disseminated intravascular coagulant response. Complement activation resulting from bacterial infection shares with selected tumors the capacity to generate or release membrane particles that lack functional adhesion receptors and hence could circulate to amplify a disseminated intravascular coagulant response. We developed a model of venous thrombosis that resulted in localized thrombus formation without disseminated intravascular coagulation. The model involves infusion of tumor necrosis factor, blockade of ◇protein◇ ◇C◇ and a partial decrease in venous flow caused by ligation of the superficial femoral vein without obstruction of the deep formal vein. Infusion of phospholipid vesicles into this model resulted in amplification of a localized thrombotic response into a consumptive response. Seven different groups of animals were studied. The first three groups established the conditions necessary to produce deep vein thrombosis. The second four groups established the conditions necessary to produce disseminated intravascular coagulation. The infusion of phospholipid vesicles plus tumor necrosis factor and anti-◇protein◇ ◇C◇ ◇antibody◇ resulted in consumption of fibrinogen, the production of thrombin/antithrombin complexes, a fall in platelet count, and venous thrombosis. Without ligation and catheterization phospholipid vesicles failed to produce the consumptive response. We conclude, therefore, that phospholipid vesicles can amplify a local thrombotic response into a consumptive response, and that vesiculation accompanying ◇inflammation◇ is one means by which localized coagulant activity may be amplified to produce disseminated intravascular coagulation.

L5 ANSWER 31 OF 41 MEDLINE
AN 96288152 MEDLINE
DN 96288152 PubMed ID: 8689765
TI Endothelial cell activation in cutaneous vasculitis.
AU Jurd K M; Stephens C J; Black M M; Hunt B J
CS Department of Haematology, St Thomas' Hospital, London, UK.
SO CLINICAL AND EXPERIMENTAL DERMATOLOGY, (1996 Jan) 21 (1) 28-32.
Journal code: DDU; 7606847. ISSN: 0307-6938.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960826
AB Markers of endothelial cell activation were measured in 28 patients presenting with various forms of limited or focal type cutaneous vasculitis. Plasma levels of tissue plasminogen activator antigen (t-PA:Ag), plasminogen activator inhibitor type 1 antigen (PAI-1:Ag) and PAI-1 activity, fibrin plate, von Willebrand factor antigen (vWF:Ag), tissue factor (TF) and soluble thrombomodulin (sTM) were measured. In comparison with the control group (n = 20) there was a significant increase in t-PA:Ag, vWF:Ag and TF ($P < 0.05$, Mann-Whitney U-test) in the cutaneous vasculitis group. This study confirms that measurable degrees of endothelial activation occur in cutaneous vasculitis. Cutaneous vasculitis includes a diverse group of clinical conditions, which are associated with ◇inflammatory◇ changes in cutaneous blood vessels with local fibrin deposition. The aetiology and pathogenesis of the majority of these entities remain unknown. Causative mediators are thought to include immune
complexes, anti-endothelial cell ◇antibodies◇, cytotoxic lymphocytes and viruses. Histologically, immune complexes and complement
are frequently detected on the vessel wall, and serologically anti-endothelial ◇antibodies◇ are often detected in patients with vasculitis and in systemic lupus erythematosus (SLE) which correlate with the severity of cutaneous vasculitis, arthritis and nephritis. Lymphocyte-mediated toxicity to endothelial cells has been reported in a small number of patients with giant cell arteritis and Takayasu's arteritis. The vascular endothelium plays a central part in the control of haemostasis. Under physiological conditions endothelial cells present an anticoagulant surface to blood constituents, partially due to surface expression of heparan sulphate and thrombomodulin (TM). Heparan sulphate binds antithrombin III (ATIII), thereby accelerating inactivation of intrinsic coagulation enzymes. Thrombomodulin is an endothelial cell surface glycoprotein which promotes anticoagulation by forming a complex with thrombin which then activates ◇protein◇ ◇C◇.
Activated ◇protein◇ ◇C◇ together with a cofactor, protein S, inactivates FVa and FVIIIa. von Willebrand factor (vWF) is synthesized by endothelial cells, stored in Weibel-Palade bodies and released into the circulation upon endothelial stimulation. vWF mediates the binding of platelets to the subendothelium and is the carrier molecule for FVIIIC. The endothelium controls fibrinolysis by producing t-PA and its inhibitor PAI-1. ◇Inflammatory◇ cytokines such as interleukin-1 (IL-1) and tumour necrosis factor (TNF) activate endothelial cells, causing a shift from an antithrombotic to prothrombotic state, including expression of tissue factor, increased synthesis of PAI-1 and decreased expression of TM. Fibrin deposition and intravascular thrombosis are seen in cutaneous

vasculitis syndromes, suggesting local endothelial cell activation. The aim of this pilot study was to assess whether perturbation of the endothelium in cutaneous vasculitis could be detected in the patients' plasma samples. If so, further studies to assess any correlation in levels of these markers with disease activity might prove useful in the future.

L5 ANSWER 32 OF 41 MEDLINE
AN 96244962 MEDLINE
DN 96244962 PubMed ID: 8656085
TI [Role of the hemostasis laboratory in the etiologic approach to deep vein thrombosis].
Place du laboratoire d'hemostase dans la demarche etiologique des thromboses veineuses profondes.
AU De Maistre E; Briquel M E; Andre E; Regnault V; Whal D; Perret C; Laprevote M C; Lecompte T
CS Laboratoire d'Hemostase et Laboratoire Universitaire d'Hematologie, Nancy.
SO JOURNAL DES MALADIES VASCULAIRES, (1996) 21 (1) 1-6. Ref: 19
Journal code: IYN; 7707965. ISSN: 0398-0499.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 199608
ED Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960801
AB Thrombophilia is characterized by an inherited or acquired defect in the blood coagulation pathway leading to an increased risk for thrombosis. The etiological approach following confirmed venous thrombotic events should rule out medical or chirurgical risk factors. Thrombophilia should be sought by laboratory tests. The recent discovery of a blood coagulation defect: inherited resistance to activated ◇protein/ ◇C/ which is found to 20% of patients with former thrombotic events has changed current laboratory approach. Deficiencies of one of the anticoagulant proteins (antithrombin III, ◇protein/ ◇C/, protein S) are found in 10% of the patients, similar to the frequency of antiphospholipid ◇antibodies/. These tests may be difficult to interpret immediately after the thrombotic event because of various factors such as ◇inflammatory/ states or anticoagulant treatments. Therefore this abnormal tests should be confirmed on a later sample analysis far from the event. The discovery of an inherited blood coagulation pathway defect may affect the duration of treatment, prophylaxis in situations with circumstantial risk factors and requires familial analysis. Inherited resistance to activated ◇protein/ ◇C/ may be associated with another inherited defect leading to an increased risk for thrombosis.

L5 ANSWER 33 OF 41 MEDLINE
AN 96075673 MEDLINE
DN 96075673 PubMed ID: 7482409
TI IL-6 upregulates protein S expression in the HepG-2 hepatoma cells.
AU Hooper W C; Phillips D J; Ribeiro M; Benson J; Evatt B L
CS Division of HIV/AIDS, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.
SO THROMBOSIS AND HAEMOSTASIS, (1995 May) 73 (5) 819-24.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199512
ED Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951206
AB Several pro-◇inflammatory/ cytokines have been shown to be important in the modulation of the procoagulant response. However, what role these cytokines may have in the regulation of coagulation inhibitors is poorly understood. While the hepatocyte is a primary site of synthesis for the anticoagulant ◇protein/ ◇C/ and S, it is also a major target cell for the proinflammatory cytokine, IL-6. We have found that stimulation of HepG-2 hepatoma cells with IL-6 (5 ng/ ml) significantly increased the production of the anticoagulant cofactor, protein S, in both a time and dose dependent fashion. This increase was seen at both the RNA and protein level. A mouse monoclonal neutralizing ◇antibody/ to human IL-6 suppressed the IL-6 effect in a concentration dependent fashion. IL-6 also increased the release of the C4b-binding protein but had no effect on ◇protein/ ◇C/ production. When combined with either dexamethasone or soluble IL-6 receptor, the IL-6 response was significantly enhanced. Oncostatin M, a functionally related cytokine, had a similar effect while other related cytokines, IL-11 and leukemia inhibitory factor, only had a marginal effect. IL-1, TGF-beta, and TNF-alpha had no significant effect on protein S production. These results indicate that IL-6 may play an important regulatory role in the anti-coagulant pathway.

L5 ANSWER 34 OF 41 MEDLINE
AN 95313010 MEDLINE
DN 95313010 PubMed ID: 7792739
TI Antinociceptive properties of protein C in a model of inflammatory hyperalgesia in rats.
AU Pichler L; Schramm W; Ulrich W; Varadi K; Schwarz H P
CS Department of Pharmacology and Toxicology, Immuno AG, Vienna, Austria.
SO THROMBOSIS AND HAEMOSTASIS, (1995 Feb) 73 (2) 252-5.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950807
Last Updated on STN: 19950807
Entered Medline: 19950727
AB We investigated the role of human ◇protein/ ◇C/ in an animal model of ◇inflammatory/ hyperalgesia. Pain was induced by intraplantar injection of carrageenan (3 mg) into the hind paw of rats. The pain threshold was measured by exerting increasing amounts of pressure (in mmHg) on the paw until a struggle reaction was observed. ◇Protein/ ◇C/ (8-800 IU/kg) was administered intravenously immediately after carrageenan. Controls received either intraplantar injections of saline (100 microliters) instead of carrageenan or carrageenan alone. Effects on pain threshold were expressed in percent of the pretreatment value. Carrageenan alone lowered the mean pain threshold after 3 h to 33.2 +/- 2.2% of the pretreatment level. Addition of ◇protein/ ◇C/ resulted in a dose-dependent rise in pain threshold towards the level observed in control animals treated with saline instead of carrageenan (pain threshold after 800 IU/kg ◇protein/ ◇C/ = 62.9 +/- 2.3% of pretreatment level), demonstrating an antinociceptive effect. ◇Protein/ ◇C/ had no effect in animals not preconditioned with intraplantar carrageenan. Thus ◇protein/ ◇C/ clearly antagonized the ◇inflammatory/ pain induced by carrageenan. The antinociceptive action of ◇protein/ ◇C/ was antagonized by injection of a monoclonal ◇antibody/ against ◇protein/ ◇C/, providing additional evidence that the effect was ◇protein/ ◇C/-mediated.

L5 ANSWER 35 OF 41 MEDLINE
AN 95159086 MEDLINE
DN 95159086 PubMed ID: 7855799
TI High affinity binding sites for activated protein C and protein C on cultured human umbilical vein endothelial cells. Independent of protein S and distinct from known ligands.
AU Bangalore N; Drohan W N; Orthner C L
CS Plasma Derivatives Laboratory, American Red Cross Holland Laboratory, Rockville, Maryland 20855.
SO THROMBOSIS AND HAEMOSTASIS, (1994 Sep) 72 (3) 465-74.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314
AB Activated ◇protein/ ◇C/ (APC) is an antithrombotic serine proteinase having anticoagulant, profibrinolytic and anti-◇inflammatory/ activities. Despite its potential clinical utility, relatively little is known about its clearance mechanisms. In the present study we have characterized the interaction of APC and its active site blocked forms with human umbilical vein endothelial cells (HUVEC). At 4 degrees C 125I-APC bound to HUVEC in a specific, time dependent, saturable and reversible manner. Scatchard analysis of the binding isotherm demonstrated a Kd value of 6.8 nM and total number of binding sites per cell of 359,000. Similar binding isotherms were obtained using radiolabeled ◇protein/ ◇C/ (PC) zymogen as well as D-phe-pro-arg-chloromethylketone (PPACK) inhibited APC indicating that a functional active site was not required. Competition studies showed that the binding of APC, PPACK-APC and PC were mutually exclusive suggesting that they bound to the same site(s). Proteolytic removal of the N-terminal gamma-carboxyglutamic acid (gla) domain of PC abolished its ability to compete indicating that the gla-domain was essential for cell binding. Surprisingly, APC binding to these cells appeared to be independent of protein S, a cofactor of APC generally thought to be required for its high affinity binding to cell surfaces. The identity of the cell binding site(s), for the most part, appeared to be distinct from other known APC ligands which are associated with cell membranes or extracellular matrix including phospholipid, thrombomodulin, factor V, plasminogen activator inhibitor type 1 (PAI-1) and heparin. Pretreatment of HUVEC with antifactor VIII ◇antibody/ caused partial inhibition of 125I-APC binding indicating that factor VIII or a homolog accounted for approximately 30% of APC binding. Studies of the properties of surface bound 125I-APC or 125I-PC and their fate at 4 degrees C compared to 37 degrees C were consistent with association of approximately 25% of the initially bound radioligand with an endocytic receptor. However, most of the radioligand appeared not to be bound to an endocytic receptor and dissociated rapidly at 37 degrees C in an intact and functional state. These data indicate the presence of specific, high affinity binding sites for APC and PC on the surface of HUVEC. While a minor proportion of binding sites may be involved in endocytosis, the identity and function of

the major proportion is presently unknown. It is speculated that this putative receptor may be a further mechanisms of localizing the PC antithrombitic system to the vascular endothelium.

L5 ANSWER 36 OF 41 MEDLINE
AN 95152033 MEDLINE
DN 95152033 PubMed ID: 7849281
TI Aspects of immunopathogenesis of rheumatoid arthritis correlated with some immunological parameters in histopathological and electronmicroscopical investigations of the articular cartilage.
AU Ciobanu A; Ciobanu I R; Halalau F; Laky D; Ionita A; Dinulescu I; Stanculescu M; Stoicescu M; Stroescu I
CS Victor Babes Institute, Bucharest, Romania.
SO ROMANIAN JOURNAL OF MORPHOLOGY AND EMBRYOLOGY, (1993 Jul-Dec) 39 (3-4) 135-44.
Journal code: A78; 9112454. ISSN: 1220-0522.
CY Romania
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950315
AB The histopathological (H. E., V. G., PAS-Alcian, Safranine 0, Gomori) and electron-microscopical investigations were carried out on twenty samples of articular cartilage taken during operations from patients with Rheumatoid Arthritis (R. A.) and from others with traumatism, as controls. Histopathologically, the rheumatoid synovial membrane is characterized by synovitis with abundant perivascular lymphoplasmocytic infiltrates. At the pannus synovia-cartilage junction we found the invasive and destructive ◇inflammatory♬ infiltrates penetrating and eroding the cartilage. The histopathological characteristics of the rheumatoid articular cartilage lie in alteration of tinctorial activity, affection of reticuline collagen network and the presence of superficial and deep cartilaginous fissures. The histopathological alterations were confirmed ultrastructurally. Immunologically we found pathological serum values regarding the immune circulating complexes (I. C. C.) (mean = 104 +/- 1.04 U), anticollagen II ◇antibodies♬ (mean = 538 +/- 5 U), reactive ◇protein♬ ◇C♬ (mean = 16.75 +/- 1.95 mg%) and orosomucoid (mean = 151.1 +/- 4.91 mg%), in seropositive R. A. The corroboration of histopathological, electronmicroscopical and immunological data show the ◇inflammatory♬ and autoimmune feature of this rheumatic disease.

L5 ANSWER 37 OF 41 MEDLINE
AN 95152032 MEDLINE
DN 95152032 PubMed ID: 7849280
TI Aspects of ankylosing spondylarthritis immunopathogenesis correlated with some immunoseric- and synovial parameters in the investigation of histopathological and electronmicroscopic alterations of the articular cartilage correlated with some immunoseric and synovial parameters.
AU Ciobanu A; Ciobanu I R; Halalau F; Laky D; Ionita A; Dinulescu I; Stanculescu M; Stoicescu M; Stroescu I; Bundaru A
CS V. Babes Institute, Bucharest, Romania.
SO ROMANIAN JOURNAL OF MORPHOLOGY AND EMBRYOLOGY, (1993 Jul-Dec) 39 (3-4) 125-34.
Journal code: A78; 9112454. ISSN: 1220-0522.
CY Romania
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950315
AB Eighteen biopsies of articular cartilage taken intraoperatory from patients with Ankylosing Spondylarthritis (AS) and from others with traumatisms (controls) were investigated using histopathological (HE, VG, PAS-Alcian, Gomori, Safranin 0), electronmicroscopic and histoenzymamologic techniques. Histopathologically, the synovitis in AS is characterized by abundant synovia lymphoplasmocytic infiltrates associated with aspects of vascular hyperplasia and fibrosis. At the pannus synovia-cartilage junction we found the invasive synovia lymphoplasmocytic infiltrates. The proteoglycan (PG) depletion is confirmed histopathologically by diminishing the Safranin 0 staining, then ultrastructurally by the existence of collagen revealing areas, whereas biochemically, by the presence of glycosaminoglycans (GAG) in serum and synovial fluid (SF). The morphological data were related to some immunological parameters involved in pathogenesis. In this way, we found pathological values of the immune circulating complexes (ICC) (serum, mean = 73.5 U; SF mean = 81.80 U) and of anti Collagen II ◇antibodies♬ (serum mean = 410 U; SF mean = 436 U). The reactive ◇protein♬ ◇C♬ acting in the phase (CRP) showed high pathological values both in serum (mean = 5.01 mg%) and in SF (mean = 3.6 mg%) of the patients with AS, emphasizing the ◇inflammatory♬ characteristics of the rheumatic disease. The presence of ICC, anticollagen II ◇antibodies♬ and GAS as well in synovia suggests that the ◇inflammatory♬ articulation in AS is a local potential antigen of collagen and proteoglycan nature.

L5 ANSWER 38 OF 41 MEDLINE
AN 94323907 MEDLINE
DN 94323907 PubMed ID: 8048002
TI Activation of hepatic proliferation-associated transcription factors by lipopolysaccharide.
AU Beauchamp R D; Papaconstantinou J; Henderson A M; Sheng H M; Townsend C M Jr; Thompson J C
CS Department of Surgery, University of Texas Medical Branch, Galveston 77555-0533.
NC PO1 DK35608 (NIDDK)
R01 DK15241 (NIDDK)
T32 DK07639 (NIDDK)
SO SURGERY, (1994 Aug) 116 (2) 367-76; discussion 376-7.
Journal code: VC3; 0417347. ISSN: 0039-6060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199408
ED Entered STN: 19940909
Last Updated on STN: 19940909
Entered Medline: 19940830
AB BACKGROUND. The hepatic acute-phase response is the result of reprogramming of gene expression in the liver. Similar acute-phase responses occur in regenerating liver after partial hepatectomy and are preceded by increases in the expression of a set of transcriptional regulatory proteins that are encoded by "immediate-early" genes. The purpose of this study was to determine whether acute systemic ◇inflammation♬ after lipopolysaccharide injection induces hepatic immediate-early genes that are induced by partial hepatectomy. METHODS. Two- to 4-month-old Balb/c mice received intraperitoneal Escherichia coli lipopolysaccharide (0111:B4; 100 micrograms), and total liver RNA, nuclear protein extracts, or total liver protein lysates were obtained at 0, 1, 3, 12, and 24 hours. RNA blot hybridization analysis was used to determine steady-state messenger RNA levels for c-jun, jun-B, jun-D, c-fos, fos-B, fra-1, nup475, and zif268. Specific nuclear protein-binding activity was determined by gel mobility shift assay. The ◇protein♬ ◇c♬ -Jun was detected by ◇antibody♬-blocking experiments, and Jun-B was detected by gel supershift assay of the activating protein (AP-1) complex. Steady-state Jun-B levels were determined by immunoblot analysis. RESULTS. Intraperitoneal injection of lipopolysaccharide is followed by induction (from fivefold to 13-fold) of c-jun, jun-B, c-fos, zif268, and nup475 messenger RNAs in the liver. Lipopolysaccharide induced increases in AP-1 and Zif268 consensus DNA-binding activity in mouse liver. The proteins c-Jun and Jun-B are detected in the AP-1 complex after administration of lipopolysaccharide. CONCLUSIONS. The induction of hepatic immediate-early genes after lipopolysaccharide is similar to that that follows partial hepatectomy. These transcription factors likely have important roles in the reprogramming of gene expression that leads to the acute-phase response.

L5 ANSWER 39 OF 41 MEDLINE
AN 94271661 MEDLINE
DN 94271661 PubMed ID: 8003387
TI Pro-thrombotic states and their diagnosis.
AU Coccheri S; Palareti G
CS Cattedra di Angiologia, Policlinico S. Orsola-Malpighi, Bologna.
SO ANNALI ITALIANI DI MEDICINA INTERNA, (1994 Jan-Mar) 9 (1) 16-21.
Ref: 29
Journal code: AUZ; 8806705. ISSN: 0393-9340.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199407
ED Entered STN: 19940729
Last Updated on STN: 19940729
Entered Medline: 19940720
AB The authors define pro-thrombotic states as conditions associated with a high frequency of thrombosis; this association is based on pathogenetic or simply clinical and epidemiological relationships. Thrombophilic states have well-defined, specific causes: antithrombin III, ◇protein♬ ◇C♬ and S and similar deficiencies for inherited thrombophilias, and lupus anticoagulant, antiphospholipid ◇antibodies♬ for the acquired forms. Another identifiable group is made up of several conditions predisposing to thrombosis (CPT) characterized by less specific and multiple mechanisms (e.g. malignancy, ◇inflammatory♬ bowel disease, nephrotic syndrome, diabetes, obesity, etc.). These conditions may induce thrombosis by themselves or contribute to its clinical onset in patients with true thrombophilic states. This is especially the case for patients who are taking contraceptive drugs, are pregnant, have undergone surgery or trauma. The term hypercoagulability states is by no means equivalent to either thrombophilia or CPT. In fact, hypercoagulability may be defined as "activation of blood coagulation" in the presence of specific markers such as fibrinopeptide A and prothrombin fragment F1 + 2. Hypercoagulability is therefore a laboratory rather than a clinical condition and can be a transient feature appearing during certain phases of thrombophilia or CPT. Lastly, conditions involving the presence of

hemostatic risk factors for atherothrombosis are simply terms used to describe a statistical-epidemiological relationship between certain hemostatic variables (fibrinogen, factor VII, PAI, etc.) involving the risk of cardiovascular morbidity and mortality but not necessarily indicating a hypercoagulability state.

L5 ANSWER 40 OF 41 MEDLINE
AN 94254889 MEDLINE
DN 94254889 PubMed ID: 8196668
TI Serum amyloid A gene expression under acute-phase conditions involves participation of inducible C/EBP-beta and C/EBP-delta and their activation by phosphorylation.
AU Ray A; Ray B K
CS Department of Veterinary Microbiology, University of Missouri, Columbia 65211.
NC DK 45144-01 (NIDDK)
SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Jun) 14 (6) 4324-32. Journal code: NGY; 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940707
Last Updated on STN: 19970203
Entered Medline: 19940624
AB Serum amyloid A (SAA) is a plasma protein whose synthesis is markedly increased in the liver during the ◇inflammatory◇ process. Previous analysis of SAA promoter function implicated the involvement of the CCAAT/enhancer-binding ◇protein◇ (◇C◇/EBP) in controlling this process. In this study, using ◇antibodies◇ against three C/EBP isoforms in DNA-binding and Western blot (immunoblot) assays, we found that in response to ◇inflammatory◇ signals, both C/EBP-delta and C/EBP-beta are induced and that their interactions with the SAA promoter element are necessary for the increased SAA gene expression. Cotransfections of liver cells with an SAA promoter-linked reporter chloramphenicol acetyltransferase gene and murine sarcoma virus-expressed C/EBP-delta or C/EBP-beta confirm such phenomena. The increased transactivating ability in the presence of the cellular phosphatase inhibitors okadaic acid and sodium orthovanadate, coupled with the observation that dephosphorylation severely inhibits the DNA-binding ability in vitro, implicates a role of phosphorylation in the regulation of the activities of the C/EBP-delta isoform. Consistent with these findings, we have detected higher levels of DNA-binding activity of C/EBP-delta prepared from cells treated with phosphatase inhibitors. We also present evidence that C/EBP-delta is a phosphoprotein. These results suggest that C/EBP-delta is regulated by phosphorylation and, in conjunction with C/EBP-beta, is one of the major proteins responsible for the increased transcription of the SAA gene in response to ◇inflammatory◇ stimuli.

L5 ANSWER 41 OF 41 MEDLINE
AN 93206267 MEDLINE
DN 93206267 PubMed ID: 8456429
TI Inflammatory and procoagulant mediator interactions in an experimental baboon model of venous thrombosis.
AU Wakefield T W; Greenfield L J; Rolfe M W; DeLucia A 3rd; Strieter R M; Abrams G D; Kunkel S L; Esmon C T; Wrobleski S K; Kadell A M; +
CS Jobst Research Laboratories, Department of Surgery, University of Michigan Medical Center, Ann Arbor 48109-0329.
SO THROMBOSIS AND HAEMOSTASIS, (1993 Feb 1) 69 (2) 164-72. Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199304
ED Entered STN: 19930507
Last Updated on STN: 19960327
Entered Medline: 19930416
AB Theoretic and in vitro evidence suggests that thrombosis and ◇inflammation◇ are interrelated. The purpose of the present study was to define the relationship between ◇inflammation◇ and deep venous thrombosis (DVT) in an in vivo model. Initiation of DVT was accomplished by administration of ◇antibody◇ to ◇protein◇ ◇C◇ (HPC4, 2 mg/kg) and tumor necrosis factor (TNF, 150 micrograms/kg); stasis; and subtle venous catheter injury. Thrombosis was assessed by thrombin-antithrombin assay (TAT), 125I-fibrinogen scanning (scan) over both the proximal and distal iliac veins, and ascending venography. Cytokines TNF, interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1), and interleukin-8 (IL-8) were measured along with differential white blood cell counts, platelet counts, fibrinogen (FIB), and erythrocyte sedimentation rates (ESR). Baboon pairs were sacrificed on day 3 (T + 3d), T + 6d, and T + 9d and veins removed. All animals developed inferior vena cava and left iliofemoral DVT by venography; no right DVT was found. TAT was elevated by T + 1hr and peaked at T + 3hrs. Left iliofemoral DVT was found at T + 1hr by scan and reached a 20% uptake difference between the affected left and nonaffected right side at T + 3hrs. TNF peaked at T + 1hr; MCP-1 peaked at T + 6hrs; IL-8 and IL-6 peaked on T + 2d; all cytokines declined to baseline. TNF and TAT elevations were found to correlate with all cytokines; elevations in IL-8 were correlated with elevations in MCP-1 and IL-6 ($p < 0.05$).(ABSTRACT TRUNCATED AT 250 WORDS)

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(FILE 'HOME' ENTERED AT 17:47:47 ON 14 JUL 2001)

FILE 'MEDLINE' ENTERED AT 17:47:54 ON 14 JUL 2001
L1 10122 S PROTEIN(W)C
L2 580623 S ANTIBOD###
L3 832 S L1(P)L2
L4 205370 S INFLAMMA?
L5 41 S L3(P)L4

L4 ANSWER 51 OF 57 MEDLINE
AN 91354517 MEDLINE
DN 91354517 PubMed ID: 1652973
TI A membrane-bound form of the acute-phase protein C-reactive protein is the
galactose-specific particle receptor on rat liver macrophages.
AU Kolb-Bachofen V
CS Abteilung fur Immunobiologie, Heinrich-Heine-Universitat Dusseldorf, BRD.
SO PATHOBIOLOGY, (1991) 59 (4) 272-5. Ref: 32
Journal code: AF6; 9007504. ISSN: 1015-2008.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199110
ED Entered STN: 19911027
Last Updated on STN: 19911027
Entered Medline: 19911008
AB Rat liver macrophages express a galactose-specific **receptor** which mediates endocytosis of particles or neuraminidase-treated blood cells. From rat serum we now have isolated a galactose-specific lectin by affinity chromatography. Comparative analysis of this serum galactose-binding protein with the galactose-specific particle **receptor** protein purified from rat liver macrophages and with the acute-phase **protein C**-reactive protein (CRP) revealed a close relation or identity of these proteins. An apparent molecular weight of 30 kilodaltons was determined for all three proteins by SDS-PAGE under reducing conditions and of about 130 kilodaltons by native PAGE. All three proteins exhibit the same pentameric, ring-shaped structure. **Antibodies** raised against the serum galactose-binding protein or against the macrophage **receptor** did cross-react. Monoclonal **antibodies** raised against rat CRP labeled liver macrophage but not hepatocyte surfaces and reacted with all three isolated proteins in a Western blot assay. Furthermore, the galactose-specific particle **receptor** could be functionally replaced by purified CRP. Northern blot analysis showed that the CRP is not synthesized in the macrophages but appears to be acquired from hepatocytes or blood. We now conclude that a membrane-bound form of CRP functions as the recycling galactose-specific particle **receptor** in rat liver Kupffer cells.

L4 ANSWER 34 OF 57 MEDLINE
AN 96125842 MEDLINE
DN 96125842 PubMed ID: 8545885
TI Binding of activated protein C to a specific receptor on human mononuclear phagocytes inhibits intracellular calcium signaling and monocyte-dependent proliferative responses.
AU Hancock W W; Grey S T; Hau L; Akalin E; Orthner C; Sayegh M H; Salem H H
CS Department of Pathology and Immunology, Alfred Hospital, Monash Medical School, Prahran, Victoria, Australia.
SO TRANSPLANTATION, (1995 Dec 27) 60 (12) 1525-32.
Journal code: WEJ; 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199602
ED Entered STN: 19960227
Last Updated on STN: 19970203
Entered Medline: 19960213
AB Upon activation, mononuclear phagocytes (Mphi) play key roles in the development of septic shock and multiple host immune responses, but details of the regulation of Mphi activation are little understood. We recently showed that the physiologic anticoagulant molecule, activated **protein C** (APC), blocks responses of human blood Mphi, alveolar Mphi, or THP-1 cells induced by LPS, IFN-gamma, or PMA, including TNF-alpha production and down-regulation of several LPS binding-related proteins. We now report a possible mechanism of action through inhibition of the rapid intracellular calcium signaling that occurs at the onset of Mphi activation, and characterization of a specific Mphi **receptor** for APC. Flow cytometry studies using Fluo-3 showed that Mph activation by Fc-**receptor** cross-linking or rIFN-gamma caused a rapid increase in free intracellular calcium, a primary event in multiple signal transduction pathways, which was blocked by pretreatment with APC. Consistent with this, addition of APC inhibited PHA-induced T cell proliferation in a dose- and time-dependent manner. Peak suppression (> 70%) required addition of APC within the first hour of 72 hr cocultures of Mphi and lymphocytes, and proliferative responses were not restored by addition of IL-2 or TNF-alpha. Biochemical studies showed that 125I-labeled APC bound specifically to M phi in a time-dependent and saturable manner. Scatchard analysis indicated there were 180,690 binding sites for APC per cell, which were of high affinity (Kd value of 12.9 mM). Binding of 125I-APC was doubled by activation of Mphi with LPS, and bound APC was not displaced by the zymogen, **protein C** (PC), or by enzymatically inactive (diisopropyl fluorophosphate- or PPACK-treated) APC, indicating an absolute requirement for the active site of APC in its binding to Mphi. APC binding was blocked by a polyclonal Ab to human PC/APC, but not by protein S, factor Va or Xa, or a polyclonal antithrombomodulin **antibody**. When 125I-APC was crosslinked to its **receptor**, immunoprecipitated and analyzed by SDS-PAGE under reducing conditions, a covalent complex (110-115 kD) of 125I-APC (62 kD) and its **receptor** was seen. In addition, a Mphi membrane protein of 50-55 kD, as determined by SDS-PAGE, was affinity-purified using an

APC-Affigel col[redacted], and confirmed by ligand bindi[redacted]g. Taken together, our findings docume[redacted] the presence of a M phi surfa[redacted]**eceptor** for APC, which appears distinct from a recently described endothelial **receptor** for PC and APC, and which may be involved in the inhibitory effects of APC on activation of human Mphi, including Mphi-dependent T cell proliferation.

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L4 ANSWER 30 OF 57 MEDLINE
AN 96302769 MEDLINE
DN 96302769 PubMed ID: 8743182
TI Infusion of phospholipid vesicles amplifies the local thrombotic response to TNF and anti-protein C into a consumptive response.
AU Taylor F B Jr; He S E; Chang A C; Box J; Ferrell G; Lee D; Lockhart M; Peer G; Esmon C T
CS Oklahoma Medical Research Foundation, Oklahoma City 73104, USA.
NC 2R01 GM37704 (NIGMS)
R37 HL30340 (NHLBI)
SO THROMBOSIS AND HAEMOSTASIS, (1996 Apr) 75 (4) 578-84.
Journal code: VQ7; 7608063. ISSN: 0340-6245.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961105
AB Inflammation often is considered a contributing factor to both thrombosis and disseminated intravascular coagulation. The molecular mechanisms that dictate which of these clinical manifestations will result from the inflammatory stimulus remain obscure. Bacterial infection and certain tumors are common initiators of the disseminated intravascular coagulant response. Complement activation resulting from bacterial infection shares with selected tumors the capacity to generate or release membrane particles that lack functional adhesion **receptors** and hence could circulate to amplify a disseminated intravascular coagulant response. We developed a model of venous thrombosis that resulted in localized thrombus formation without disseminated intravascular coagulation. The model involves infusion of tumor necrosis factor, blockade of **protein C** and a partial decrease in venous flow caused by ligation of the superficial femoral vein without obstruction of the deep formal vein. Infusion of phospholipid vesicles into this model resulted in amplification of a localized thrombotic response into a consumptive response. Seven different groups of animals were studied. The first three groups established the conditions necessary to produce deep vein thrombosis. The second four groups established the conditions necessary to produce disseminated intravascular coagulation. The infusion of phospholipid vesicles plus tumor necrosis factor and anti-**protein C antibody** resulted in consumption of fibrinogen, the production of thrombin/antithrombin complexes, a fall in platelet count, and venous thrombosis. Without ligation and catheterization phospholipid vesicles failed to produce the consumptive response. We conclude, therefore, that phospholipid vesicles can amplify a local thrombotic response into a consumptive response, and that vesiculation accompanying inflammation is one means by which localized coagulant activity may be amplified to produce disseminated intravascular coagulation.